

Effective Management of Patient Recruitment Organizations

By Beth D. Harper

Introduction

As the clinical research environment becomes more and more challenging, the need for a robust patient recruitment and retention plan is becoming a necessity rather than a luxury. The strategy may include outsourcing key activities to a Patient Recruitment Organization or "PRO," (a term not to be confused with "Patient Reported Outcomes"). Over 60 PROs exist today¹, and the number continues to grow.

As with any outsourced activity, the expectations should be clear for what services will be provided, what deliverables can be anticipated, and how sponsor-CRO-PRO-site communications will be managed.

While some sponsors and CROs have their own internal patient recruitment departments, this article will discuss external vendors. It will also use the terms "patient" and "subject" interchangeably.

PRO Services

PROs provide a variety of strategic and tactical services to the biopharmaceutical and medical device industries. While some vendors contract directly with sites, most work for the sponsor or CRO to provide services on behalf of multiple sites in a given clinical trial. PROs can employ a multitude of tactics to build study awareness with traditional and digital media. PROs might also help with patient retention and compliance, e.g., with visit reminders and transportation assistance. Some PROs can support global programs across multiple therapeutic areas, while others offer regional or disease-specific expertise. Niche vendors might specialize in mining proprietary patient databases, supporting community outreach events, working with advocacy groups, providing data analytics for study feasibility and recruitment planning, or any number of other services.

When to Engage a PRO

While most trials ultimately meet their enrollment goals, it often can take twice as long as expected.² This finding suggests that many study sponsors could benefit from PRO assistance in creating a reliable patient recruitment and retention plan.

A good rule of thumb is to involve a PRO if the sites, on average, estimate they will need to recruit 30% or more of the patients from outside sources. A PRO can help develop the materials and support outreach and awareness efforts to "fill the funnel" of potential candidates. If the sites anticipate high consent refusal or drop-out ratios, a PRO can assist with patient education and retention activities.

It is common to engage a PRO when enrollment has faltered and the study needs to be rescued. However, it is best to involve a PRO early in the study design phase. During feasibility assessment, the PRO can help anticipate potential barriers to enrollment and retention. The PRO can advise on country allocation and site selection criteria. It can help develop a reliable recruitment and retention plan that will avoid time and budget overruns. The earlier the PRO is involved, the more time it will have to develop study branding and creative materials and messaging, which will need to go through time-consuming internal and external review, translation and approval.

Assessing PRO Performance

Assuming the sponsor or CRO has performed sufficient due diligence to select a PRO well-suited to the needs of the study, the next issue is how best to evaluate the PRO's performance. Clear, precise and appropriate expectations for deliverables and the PRO's role in managing conversion of referred patients are required. Because the PRO does not control the entire process, especially at the sites, measuring its performance is more complicated than just counting enrolled subjects. It is therefore important for the sponsor and PRO to establish mutually acceptable measures for assessing the PRO's performance.

PROs employ a variety of tactics to create awareness for trials and encourage patients to seek more information and enter into a pre-screening process to determine their eligibility. Prescreening can be performed via web or phone-screening questionnaires. The PRO then refers each pre-qualified candidate to a local site.

It is then the site's responsibility to follow up on the referrals. The site may perform additional telephone pre-screening, obtain medical records to document the presence or absence of certain eligibility criteria, and then schedule the patient for a screening visit. Prospective subjects may fall through many cracks. The site may not be able to follow up on referrals in a timely manner. The candidates may not show up for their appointments, they might decline to give consent, or their lab tests or other criteria might render them ineligible for participation.

The PRO should be able to provide very accurate metrics for the performance of recruitment campaigns, e.g., advertisements run and exposures achieved, and percentage of pre-screened candidates who are referred to the sites, but somewhat less accurate estimates of site follow-up and ultimate enrollment the patients.

The important point here is that the PRO may have little or no control over the conversion of referred patients into consented and enrolled subjects. However, if the PRO is involved in selecting and training the sites or managing their enrollment processes, it may be able to influence conversion ratios to a greater degree. For example, through weekly phone calls to the sites or even periodic site visits, PRO site liaisons or site managers may work with the sites to create a more efficient process. For example the PRO may agree with a site to set up blocks of time in which the PRO itself can schedule the first patient visits. Or, the PRO may employ a "warm transfer" process, whereby the PRO transfers patient telephone calls to a site for additional screening and first-visit scheduling. In any case, an experienced PRO should be able to estimate, with some degree of accuracy, what percentage of referred patients will move through the recruitment pipeline and eventually enroll, even if it is not directly involved in the process.

It is a rare patient recruiting plan that proceeds entirely as expected, so quick adjustments are essential. Given adequate access to study data and site personnel, the PRO should be able to assess progress, diagnose bottlenecks, and provide solutions. The study sponsor should meet with the PRO periodically, e.g., monthly, to review progress and make adjustments to the recruitment and retention plan.

Performance-Based Pricing

It is tempting to hold the PRO accountable for the actual enrollment and randomization of subjects into clinical trials. However, as discussed above, PROs seldom control the entire process, so they can be reluctant to accept financial risk tied to enrollment. That said, there are some opportunities to share risk with performance-based pricing. The metrics used are called "payment markers." To be effective, a payment marker must be relevant, objective, measurable, understandable, and considered by both parties to be a fair measure of performance.³

Typical performance metrics for evaluating PRO performance include the following:

- Number of responses by region to each of the various recruitment tactics
- % of the respondents who pass the pre-screening questionnaire and are referred to the sites
- % of referrals that are scheduled by sites for visits
- % of scheduled referrals that are consented
- % of consented subjects that are randomized
- % of patients contributed by the PRO versus the sites

Some advocates of performance-based pricing suggest that some of the PRO's variable costs (e.g., their project management fees) be placed at risk, recognizing that their costs to develop creative materials and implement the awareness campaigns must be incurred regardless of their success. It is reasonable to ask a PRO to put its profits and internal costs at risk, but less reasonable to ask it to take risks based on costs incurred with other parties. For example, say the PRO charges \$50,000 for market research, to develop creative materials, and to translate, produce and ship the materials to the sites. On top of this charge, the PRO charges \$350,000 to place various outreach activities in media channels. The PRO charges an additional \$50,000 to manage the campaigns (adjust the placement of ads based on how they are performing, follow-up with the sites on patient referrals, and so forth). The sponsor may have to accept that the creative development and media placement costs are "sunk costs." Those costs will be incurred regardless of whether the sites make effective use of the referrals. But the sponsor may work with the PRO to put some of their project management fees "at risk" to ensure that the PRO works efficiently with the sites to get the most out of their referrals. The sponsor's objective in performance-based pricing should be to motivate the PRO's performance without creating an unreasonable level of risk for the PRO.

Evaluating the return on investment for using a PRO is a multi-faceted and complex process⁴ but, at minimum, some attention should be given to establishing reasonable performance parameters, regardless of whether the contract includes risk-based pricing.

Sponsor-CRO-PRO-Site Interactions

When multiple parties are involved in any process, responsibilities and communication pathways must be clearly articulated. When a PRO is involved in patient recruiting and retention, there is no one right approach; it depends on the characteristics of the study, the responsibilities of the parties, and their preferred approach to communications.

At one extreme, the PRO generates patient referrals or a list of patients for sites to contact, and has no further responsibility. At the other extreme, the PRO takes complete responsibility for designing the patient recruitment and retention plan, creating the materials, selecting the sites, and managing the site-level recruitment activity. In the middle, the PRO might create a study website and generate referrals but depend on a CRO's site monitors to serve as the single point of contact with the sites.

Without a clear statement (and implementation) of responsibilities and communication pathways, a study can go seriously wrong. Take, for instance, the situation in which a PRO develops a robust kit of materials for the site, translated and customized to each site's needs, which it ships to the sites. A particular site is underperforming because it never received the materials and assumed they were delayed. The PRO does not have the authority to contact the site to investigate. The CRA's site monitor does not know she is responsible for verifying receipt of the materials at the site. The sponsor assumes the CRO

and PRO are handling the problem. As a result, the cause of the problem is never addressed, and no one ever identifies its cause.

Conclusion

Effective use of a PRO for patient recruitment and retention starts with careful selection of a vendor well-suited for the specific needs of the study. Once one (or more) PROs have been secured, they are most likely to be successful if the following steps are taken:

- Involve the PRO early in the protocol development and study-planning process.
- Establish clear and realistic performance expectations based on well-identified deliverables.
- Periodically assess the PRO's performance and work with it to address any problems that emerge.
- Ensure that all parties understand their responsibilities and communication pathways.

References

1. Clinical Performance Partners, Inc., independent research, 2012
2. Tufts CSDD Impact Report: January/February 2013, as reported in <http://www.fiercebiotech.com/node/328735/print>
3. "Guest Commentary: Risk-Share Models in Patient Recruitment – An Insider's View of Metrics and Payment Markers." April 9, 2010, as reported in: <http://www.centerwatch.com/news-online/article/869>
4. Malcolm, R. Centralized Patient Recruitment: Effectiveness and Cost Effectiveness," as reported in: <http://www.ngpharma.com/article/Centralized-Patient-Recruitment-Effectiveness-and-Cost-Effectiveness>

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